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Proposed Re-evaluation Decision

Ethofumesate

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Proposed Re-evaluation Decision

After a re-evaluation of the herbicide ethofumesate, under the authority of the *Pest Control Products Act*, Health Canada's *Pest Management Regulatory Agency* (PMRA) is proposing continued registration of ethofumesate products for sale and use in Canada.

An evaluation of available scientific information found that ethofumesate products do not present unacceptable risks to human health or to the environment when used according to label directions. As a condition of the continued registration of ethofumesate uses, new risk reduction measures must be included on the labels of all products. Additional data are being requested as a result of this re-evaluation.

The PMRA's pesticide re-evaluation program considers potential risks, as well as the value, of pesticide products, to ensure they meet modern standards established to protect human health and the environment.

This proposal affects all end-use products containing ethofumesate registered in Canada. Once the final re-evaluation decision is made, the registrants will be instructed on how to address any new requirements.

This *Proposed Re-evaluation Decision* is a consultation document[1] that summarizes the science evaluation for ethofumesate and presents the reasons for the proposed re-evaluation decision. It also proposes additional risk reduction measures to further protect human health and the environment.

The information is presented in two parts. The Overview describes the regulatory process and key points of the evaluation, while the Science Evaluation provides the detailed technical information on the assessment of ethofumesate.

The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document. Please forward all comments to Publications (please see contact information indicated on the cover page of this document).

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[1] "Consultation statement" as required by subsection 28 (2) - *Pest Control Products Act* 2002 (http://laws.justice.gc.ca/en/P-9.01/92455.html)

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Overview

What Does Health Canada Consider when Making a Re-evaluation Decision?

The PMRA is re-evaluating active ingredients and their uses to determine their continuing acceptability in relation to human health, the environment and value. Ethofumesate is one of the active ingredients to be re-evaluated during the current re-evaluation cycle. Regulatory Directive DIR2001-03, *PMRA Re-evaluation Program*, presents the details of the re-evaluation activities and program structure.

Ethofumesate has been re-evaluated under the Re-evaluation Program 1, which relies as much as possible on foreign reviews, typically, United States Environmental Protection Agency (USEPA) Reregistration Eligibility Decision (RED) documents. For products to be re-evaluated under Program 1, there must exist a suitable foreign review that meets the following conditions:

- it covers the main science areas, such as human health and the environment, that are necessary for Canadian regulatory decisions;
- it addresses the active ingredient and the main formulation types registered in Canada; and
- it is relevant to registered Canadian uses.

Based on the outcome of foreign reviews, the PMRA will propose, under Program 1, a regulatory decision and appropriate risk reduction measures for Canadian uses of an active ingredient. In this decision, the PMRA takes into account the Canadian use pattern and issues (e.g. the Federal Toxic Substances Management Policy (TSMP)). A review of the chemistry of Canadian products is also conducted.

The USEPA conducted a re-evaluation of ethofumesate and published its conclusions in a 2005 RED. On the basis of health and environmental risk assessments, the USEPA concluded that ethofumesate was eligible for reregistration with implementation of risk reduction measures. Based on the comparison of US and Canadian use patterns, the USEPA assessments described in this RED document were considered an adequate basis for the proposed Canadian re-evaluation decision.

For more details on the information presented in this overview, please refer to the Science Evaluation section of this consultation document.

What is Ethofumesate?

Ethofumesate is a herbicide used to control grasses and broadleafed weeds in sugar beets. Ethofumesate is applied using ground application (band or broadcast spray) by farm workers or professional applicators.

Health Considerations

Can Approved Uses of Ethofumesate Affect Human Health?

Additional risk reduction measures are required on ethofumesate labels. Ethofumesate is unlikely to affect your health when used according to revised label directions.

Exposure to ethofumesate may occur through consumption of food and water, working as a mixer/loader/applicator or by entering treated sites. When assessing health risks, two key factors are considered: the levels at which no health effects occur, and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (e.g. children and nursing mothers). Only those uses where exposure is well below levels that cause no effects in animal testing are considered acceptable for continued registration.

The USEPA concluded that ethofumesate was unlikely to affect human health, provided that risk reduction measures were implemented. These conclusions were considered applicable to the Canadian situation, and equivalent risk reduction measures are required.

Maximum Residue Limits

The *Food and Drugs Act* prohibits the sale of adulterated food, that is, food containing a pesticide residue that exceeds the established maximum residue limit (MRL). Pesticide MRLs are established for *Food and Drugs Act* purposes through the evaluation of scientific data under the *Pest Control Products Act*. Each MRL value defines the maximum concentration in parts per million (ppm) of a pesticide allowed in/on certain foods. Food containing a pesticide residue that does not exceed the established MRL does not pose an unacceptable health risk.

Ethofumesate is currently registered in Canada for use on sugar beets. Ethofumesate may be used in other countries on other crops imported into Canada. There are no specific Canadian MRLs established for ethofumesate. Where no specific MRL for a pest control product has been established in the Food and Drug Regulations, subsection B.15.002(1) applies. This requires that residues not exceed 0.1 ppm, which has been considered a general MRL for enforcement purposes. However, changes to this general MRL may be implemented in future, as indicated in the Discussion Document DIS2006-01, *Revocation of the 0.1 ppm as a General Maximum Residue Limit for Food Pesticide Residues [Regulation B.15.002(1)]*. If and when the general MRL is revoked, a transition strategy will be established to allow permanent MRLs to be promulgated.

Environmental Considerations

What Happens When Ethofumesate is Introduced Into the Environment?

Additional risk reduction measures are required on ethofumesate labels. Ethofumesate is unlikely to affect non-target organisms when used according to revised label directions.

Non-target organisms (e.g. birds, mammals, insects, aquatic organisms and terrestrial plants) may be exposed to ethofumesate in the environment. Environmental risk is assessed by the risk quotient method, in which a risk quotient (RQ) is calculated as the ratio of the estimated environmental concentration (EEC) to the relevant effects endpoint of concern. The resulting RQs are compared to corresponding levels of concern (LOCs). An RQ less than the LOC is considered a negligible risk to non-target organisms, whereas, an RQ greater than the LOC indicates some degree of risk.

The USEPA concluded that the reregistration of ethofumesate was acceptable provided risk reduction measures to further protect the environment were implemented. These conclusions were considered applicable to the Canadian situation, and equivalent risk reduction measures are required. Furthermore, the PMRA will require aquatic and terrestrial buffer zones for formulations of ethofumesate to protect aquatic organisms and terrestrial plants from spray drift.

Measures to Minimize Risk

Registered pesticide product labels contain specific directions for use which include risk-reduction measures to protect human and environmental health. These directions must be followed by law. As a result of the re-evaluation of ethofumesate, further risk reduction measures are proposed in addition to those already identified on existing ethofumesate product labels. These additional measures are designed to further protect human health and the environment and are summarized as follows:

Human Health

- To protect mixer/loader/applicators: additional protective equipment
- To protect workers re-entering treated sites: a restricted-entry interval

Environment

- To reduce potential surface and groundwater contamination: additional advisory label statements
- To protect non-target sensitive aquatic and terrestrial plants: buffer zones for aquatic and terrestrial habitats.

What Additional Scientific Information is Being Requested?

Data are required as a condition of continued registration under Section 12 of the *Pest Control Products Act*. The registrants of this active ingredient are required to provide these data or an acceptable scientific rationale within the time specified in the decision letter that will be sent to registrants of the technical active ingredients by the PMRA.

The PMRA based the buffer zone calculations on limited toxicity data. Consequently, the buffer zones required in this document are interim. Additional data are requested to calculate buffer zone distances for the protection of sensitive aquatic habitats. Data are requested to confirm that the proposed interim terrestrial buffer zones adequately protect sensitive aquatic habitats. Appendix I lists all data requirements.

Next Steps

Before making a final re-evaluation decision on ethofumesate, the PMRA will consider all comments received from the public in response to this consultation document. The PMRA will then publish a *Re-evaluation Decision*[2] document which will include the decision, the reasons for it, a summary of comments received on the proposed decision, and the PMRA's response to these comments.

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[2] "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act* (http://laws.justice.gc.ca/en/P-9.01/92455.html)

Science Evaluation

1.0 Introduction

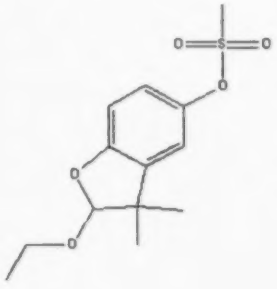
Ethofumesate is a herbicide that inhibits mitosis and reduces photosynthesis and respiration.

Following the re-evaluation announcement for ethofumesate, the registrant of the technical grade active ingredient in Canada indicated they would continue to support all uses included on the labels of commercial end-use products currently registered in Canada.

The PMRA used recent assessments of ethofumesate from the United States Environmental Protection Agency (USEPA). The USEPA Reregistration Eligibility Decision (RED) document for ethofumesate, dated September 2005, as well as other information on the regulatory status of ethofumesate in the United States, can be found on the USEPA's website at www.epa.gov/pesticides/reregistration/status.htm.

2.0 The Technical Grade Active Ingredient, Its Properties and Uses

2.1 Identity of the Technical Grade Active Ingredient

Common Name:	Ethofumesate
Function:	Herbicide
Chemical Name	
1 **International Union of Pure and Applied Chemistry (IUPAC):**	(±)2-ethoxy-2,3-dihydro-3,3-dimethylbenzofuran-5-yl methanesulfonate
2 **Chemical Abstracts Service (CAS):**	(±)2-ethoxy-2,3-dihydro-3,3-dimethyl-5-benzofuranyl methanesulfonate
CAS Registry Number:	26225-79-6
Molecular Formula:	$C_{13}H_{18}O_5S$
Structural Formula:	

Molecular Weight:	286.3	
Purity of the Technical Grade Active Ingredient (TGAI):	97.7 96.0 lower limit 100.0 upper limit	98.0 95.0 lower limit 100.0 upper limit
Registration Number:	20364	28117

Based on the manufacturing process, the product is not expected to contain impurities of human health or environmental concern as identified in Regulatory Directive DIR98-04, *Chemistry Requirements for the Registration of a Technical Grade of Active Ingredient or an Integrated System Product*, Section 2.13.4 or Toxic Substances Management Policy (TSMP) Track 1 substances as identified in Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*, Appendix II.

2.2 Physical and Chemical Properties of the Technical Grade Active Ingredient

Property	Result
Vapour pressure	0.12 to 0.65 mPa
Henry's law constant	3.7×10^{-3} to 6.8×10^{-3} Pa m^3 mol^{-1}
Solubility in water	50.0 mg/L
n-octanol–water partition coefficient	log K_{ow} = 2.7

2.3 Comparison of Use Patterns in Canada and the United States

Ethofumesate is a herbicide registered in Canada for the control of certain grasses and broadleaf weeds. It acts by the inhibition of mitosis in addition to the reduction of photosynthesis and respiration. It is used on sugar beets and is applied at pre-planting, at planting or pre-emergent. Ethofumesate is applied once a year with an application rate of up to 3.96 kg a.i./ha on sugar beets. The end-use products are formulated as emulsifiable concentrates or suspensions and are applied by ground application only (band or broadcast spray).

A comparison of US and Canadian use patterns was conducted. The Canadian formulation type of end-use products and supported use site are among those registered in the US. The Canadian supported maximum application rates are equivalent to those in the US. The Canadian potential application methods are among those registered in the US. Based on this, it was concluded that the USEPA RED for ethofumesate is an adequate basis for the re-evaluation of the Canadian uses of ethofumesate.

The current use is being supported by the registrant and was therefore considered in the re-evaluation of ethofumesate. Appendix II lists all ethofumesate products registered under the authority of the *Pest Control Products Act*.

3.0 Impact on Human Health and the Environment

The USEPA conducted a re-evaluation of ethofumesate and published its conclusions in a 2005 RED. In this document, they concluded that the end-use products formulated with ethofumesate met the safety standard under the US *Food Quality Protection Act* (FQPA) and would not pose unreasonable risks or adverse effects to humans and the environment if used according to the amended labels of all end-use products containing ethofumesate.

3.1 Human Health

Toxicology studies in laboratory animals describe potential health effects resulting from various levels of exposure to a chemical and identify dose levels where no effects are observed. Unless there is evidence to the contrary, it is assumed that effects observed in animals are relevant to humans and that humans are more sensitive to the effects of a chemical than the most sensitive animal species.

Exposure to ethofumesate may occur through consumption of food and water, working as a mixer/loader/applicator or by entering treated sites. When assessing health risks, two key factors are considered: the levels where no health effects occur, and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (e.g. children and nursing mothers).

3.1.1 Occupational Exposure and Risk Assessment

Occupational risk is estimated by comparing potential exposures, with the most relevant endpoint from toxicology studies being used to calculate a margin of exposure (MOE). This is compared to a target MOE incorporating safety factors protective of the most sensitive subpopulation. If the calculated MOE is less than the target MOE, it does not necessarily mean that exposure will result in adverse effects, but measures to mitigate risk would be required. The toxicological endpoints selected by the USEPA for assessment of risk from occupational exposure are summarized in Appendix III.

Workers can be exposed to ethofumesate through mixing, loading or applying the pesticide, and when re-entering a treated site to conduct activities such as scouting and/or handling of treated crops.

3.1.1.1 Mixer/Loader/Applicator Exposure and Risk

In the US, occupational uses of ethofumesate include field/row crops (beets, carrots), and sod farms, lawns and golf courses. The USEPA did not perform an acute occupational risk assessment as no endpoint of concern was identified and based on the use pattern, there were no acute occupational exposure scenarios.

The USEPA estimated short- and intermediate-term exposure to ethofumesate during mixing/loading and application to sugar beets and considered that there were no chronic occupational scenarios. The USEPA identified 16 mixer/loader/applicator exposure scenarios for which short- and intermediate-term exposure to ethofumesate could occur from various types of application equipment. The following are relevant to the Canadian situation.

- Mixing/loading: Liquids for groundboom application to sugar beets;
- Application: Groundboom spray application on sugar beets.

Handler exposure analyses were performed using the Pesticides Handlers Exposure Database (PHED), assuming minimum (long-sleeved shirt and long pants) and baseline (long-sleeved shirt, long pants and gloves) personal protective equipment (PPE) to estimate potential exposure to ethofumesate from use in the above exposure scenarios at a maximum application rate of 4.2 kg a.i./ha. The USEPA assumed that 200 acres (80 hectares) of sugar beets would be treated by groundboom in a day.

For short- and intermediate-term dermal and inhalation exposure for the general population, the USEPA used a NOAEL of 190 mg/kg bw/day from a 90-day oral toxicity study in rats. A NOAEL of 30 mg/kg bw/day was used for short- and intermediate-term dermal and inhalation exposure for females (age 13–49 years), based on a developmental toxicity study in rabbits. The inhalation and dermal absorption rates were assumed to be 100%.

Risk for both male and female mixers/loaders was found to be acceptable (i.e. MOE = 100 for females 13–49 years; MOE = 730 for males) with the following PPE: long-sleeve shirt, long pants, shoes, socks and gloves. Risk for applicators wearing baseline PPE (long-sleeve shirt, long pants, shoes and socks) was also considered acceptable (i.e. MOE = 160 for females 13–49 years; MOE = 1200 for males).

The RED adequately addressed potential exposure scenarios associated with the Canadian uses of ethofumesate, and conclusions derived from the RED are considered applicable to the Canadian situation. Based on this, the PMRA requires baseline protective equipment in addition to wearing chemical resistant gloves during mixing and loading to further protect workers. Additional instructions concerning good hygiene practices are also required on labels. The proposed label amendments are listed in Appendix IV.

3.1.1.2 Postapplication Exposure and Risk

The postapplication occupational risk assessment considered exposures to workers entering treated sites. Postapplication exposure analyses were performed using chemical-specific dislodgeable foliar residue (DFR) default values and activity-specific transfer coefficients (TC) to estimate postapplication exposure resulting from contact with treated foliage at various times after application. DFR data include the amount of residue that can be dislodged or transferred from a surface, such as the leaves of a plant. A TC is a factor that relates worker exposure to dislodgeable residues. TCs are specific to a given crop and activity combination (e.g. hand harvesting apples, scouting late season cotton) and reflect standard agricultural work clothing

worn by adult workers. Postapplication exposure activities include harvesting, thinning, pruning, scouting and irrigating trees. Assumptions used in the US risk assessment included exposure following the maximum rate of 4.2 kg a.i./ha for low, medium and high exposure activities. Results indicated that for high exposure activities for the general population working with sugar beets, the target MOE (Target MOE = 100) was reached at 3 days after treatment (DAT), and at 0 DAT for medium and low exposure activities. For females (age 13–49 years), the target MOE for low exposure activities was reached at 0 DAT, and for medium and high exposure activities it was reached at 17 and 22 DAT, respectively. The USEPA concluded that since ethofumesate was used preplant, pre-emergence, or postemergence, medium and high exposure activities would be unlikely to occur based on the use pattern. The USEPA required a 12 hour REI, based on the acute toxicity of the active ingredient for uses that were within the scope of the Workers Protection Standard (WPS).

The RED adequately addressed potential exposure scenarios associated with the Canadian uses of ethofumesate, and conclusions derived from the RED are considered applicable to the Canadian situation. Based on this, the PMRA requires a restricted-entry interval (REI) of 12 hours to further protect workers from postapplication exposure. Additional instructions concerning good hygiene practices are also required on labels. The proposed label amendments are listed in Appendix IV.

3.1.2 Non-Occupational Exposure and Risk Assessment

3.1.2.1 Residential Exposure

Residential exposure is estimated using the MOE approach as explained for occupational exposure and risk assessment in Section 3.1.1 above. The toxicological endpoints selected by the USEPA for assessment of risk from residential exposure are summarized in Appendix III.

Homeowners can be exposed to ethofumesate through mixing, loading and applying the pesticide, and when re-entering a treated site. Toddlers can be exposed via "hand-to-mouth" and "object-to-mouth" activities and through incidental soil ingestion.

There are no residential uses registered in Canada and no potential residential exposure scenarios.

3.1.2.2 Exposure from Food and Drinking Water

Acute dietary risk is calculated considering the highest ingestion of ethofumesate that would be likely on any one day, and using food consumption and food residue values. A statistical analysis allows all possible combinations of consumption and residue levels to be combined to estimate a distribution of the amount of ethofumesate residue that might be consumed in a day. A value representing the high end (99.9th percentile) of this distribution is compared to the acute reference dose (ARfD), which is the dose at which an individual could be exposed on any given day and expect no adverse health effects. When the expected intake of residues is less than the ARfD, then acute dietary exposure is considered acceptable.

The USEPA did not identify an appropriate acute endpoint of concern for the general public, however an acute dietary risk endpoint for females (ages 13–49 years old) was found with a NOAEL of 30 mg/kg bw/day from a developmental toxicity study in rabbits. The US set the acute population adjusted dose (aPAD) for females (ages 13–49 years old) at 0.3 mg/kg bw/day.

Chronic dietary risk is estimated by determining how much of a pesticide residue may be ingested with the daily diet and comparing this potential exposure to an acceptable daily intake, which is the dose at which an individual could be exposed over the course of a lifetime and expect no adverse health effects. The acceptable daily intake is referred to as the ADI in Canada, and, in the RED, it was expressed as the chronic population adjusted dose (cPAD). The ADI is based on a relevant endpoint from toxicology studies and on safety factors protective of the most sensitive subpopulation (see Appendix III).

A chronic dietary risk endpoint for the general population including infants and children based on a chronic oral toxicity/carcinogenicity study in rats was selected. The NOAEL was 127 mg/kg bw/day and the USEPA set the cPAD at 1.3 mg/kg bw/day for the general population. For females (ages 13–49 years old) the cPAD was set at 0.3 mg/kg bw/day (from the developmental toxicity study mentioned above).

Ethofumesate is very mobile in sand and moderately mobile in most other soils. Degradate mobility is similar to that of parent ethofumesate. No water monitoring data was available for ethofumesate, therefore Screening Concentration in Ground Water (SCI-GROW) was used to model estimates for the acute and chronic concentrations of ethofumesate in shallow groundwater. The model used a maximum application rate of 3.3 kg a.i./ha and a maximum number of applications per crop (applied 3x to turf in Florida). A value of 8.4 µg/L was used for both the peak and annual average value. This concentration was applied to all exposure scenarios regardless of duration of exposure as SCI-GROW calculates only the 90-day average value.

From a Tier II drinking water assessment using the model Pesticide Root Zone Model and the Exposure Analysis Modeling System (PRZM/EXAMS), the USEPA reported modelling results for the maximum surface water-derived drinking water concentrations for ethofumesate. The maximum estimated surface water-derived drinking water concentration for the use of ethofumesate was 203.1 µg/L (used for the acute analysis) using the Florida vegetable scenario (2.2 kg a.i./ha, 2 applications). The maximum 1 in 10 year annual average concentration was 39.6 µg/L (used for the chronic analysis) from the Florida turf scenario (3.4 kg a.i./ha, 3 applications). It should be noted that the USEPA also calculated the 30-year mean concentration was found to be 26.0 µg/L using the Minnesota sugar beet scenario with a maximum application rate of 3.75 lb a.i./acre (4.2 kg a.i./ha) with a maximum of one application per year.

The US assessment used was a conservative estimate of exposure based on modelling, using maximum estimates for drinking water concentrations and food exposures. Therefore, the USEPA assessment is considered applicable to the Canadian situation.

3.1.2.4 Aggregate Risk Assessment

Aggregate risk combines the different routes of exposure to ethofumesate (i.e. from food, water and residential exposures).

Acute and chronic aggregate risk assessments are comprised of contributions from food and drinking water exposures.

Short-term and intermediate aggregate risk assessments are comprised of contributions from food, drinking water and non-occupational exposure (dermal, inhalation).

The USEPA performed an unrefined acute and chronic Tier 1 aggregate risk assessment for ethofumesate using the following:

- tolerance level residues,
- the Dietary Exposure Evaluation Model software with the Food Commodity Intake Database (DEEM-FCID™, Version 2.03),
- default processing factors for dried beef, processing factors from sugar beet processing studies,
- 100% crop treatment for all commodities, and
- estimated environmental concentrations in surface water generated by PRZM/EXAMS (203.1 µg/L and 39.6 µg/L).

Aggregate acute exposure estimates were below the Agency's level of concern (5% of the aPAD for the subpopulation of concern, females ages 13–49 years old). The contribution of food or food forms to this estimate was 2.1%. No acute endpoint of concern was identified for the general population and infants. The chronic aggregate exposure was found to be <1% of the cPAD for all population subgroups and below the USEPA's level of concern.

The dietary risk assessments performed by the USEPA are relevant to the Canadian situation as the dietary food exposure assessment utilized tolerance level residues and 100% crop treatment information and included commodities for which ethofumesate is registered in Canada (sugar beets, sugar beet tops). The drinking water component of the risk assessment used screening-level model estimates of water concentrations, and was based on conservative assumptions such as maximum application rates for agricultural crops, which are higher than the maximum Canadian application rate on sugar beets.

Overall, the Canadian potential aggregate exposure scenarios were adequately addressed by the USEPA aggregate risk assessment. Therefore, the USEPA aggregate exposure conclusions are considered applicable to the uses of ethofumesate in Canada.

3.1.3 Cumulative Effects

The USEPA has not determined whether ethofumesate has a common mechanism of toxicity with other substances or whether it shares a toxic metabolite produced by other substances. Therefore, it was assumed that ethofumesate does not share a common mechanism of toxicity with other substances, and a cumulative risk assessment was not required.

3.2 Environment

3.2.1 Environmental Risk Assessment

The RED document indicated that ethofumesate is very mobile in sand with a K_d of 0.73 and moderately mobile in most other soils with K_ds ranging from 2.35–6.16. The degradates displayed mobilities similar to that of the parent ethofumesate. Terrestrial field data showed a half-life of 100 days for ethofumesate with no detection of ethofumesate below 12 inches.

The USEPA concluded that the major route of dissipation for ethofumesate in surface soil appeared to be photodegradation (half-life 28–31 hours in water; 165 hours in soil). Below the soil surface, ethofumesate appeared to be stable. The US indicated that dissipation could occur by microbial metabolism (aerobic half-life 83–253 days). Ethofumesate was stable to hydrolysis and anaerobic soil metabolism.

To assess the ecological risk of ethofumesate to aquatic non-target plants and animals, the USEPA calculated risk quotients (RQs) based on appropriate toxicity endpoints and expected environmental concentrations (EECs) and compared the resulting RQs to corresponding levels of concern (LOCs). Aerial application was considered in the modelling as this typically results in the highest amount of spray drift (sugar beet - 5% spray drift). The Tier II PRZM/EXAMS concentration of ethofumesate in surface water for use in the aquatic ecological assessment was 52.7 µg/L for the Minnesota sugar beet scenario.

From the ecological risk assessment, only the acute endangered species LOC for freshwater fish (rainbow trout) was exceeded when products containing ethofumesate were used on sugar beets. There were no acute risks of concern for freshwater invertebrates, estuarine/marine fish or estuarine/marine invertebrates. Nor were there chronic concerns for freshwater fish or freshwater invertebrates.

For the ecological risk assessment for terrestrial animals, the USEPA predicted the maximum and mean residue levels on food items (i.e. vegetative matter and insects) based on maximum label rates for spray applications, using the ELL-FATE model. Using these values, RQs were calculated and compared to LOCs.

In the terrestrial risk assessment, the USEPA calculated RQs and reported that there were no potential oral acute risks expected for birds. As for endangered species, the possibility of risk was very minimal. It was reported that birds were expected to be at minimal chronic reproductive risk from exposures to ethofumesate. In addition, the acute and chronic risks for mammals were considered small. The USEPA did not quantify risks to terrestrial non-target insects and RQs were not calculated for these organisms.

For terrestrial plant exposure to ethofumesate and the corresponding risk assessment, EECs were calculated based on spray drift and run-off. The USEPA used the TERR_PLANT program to calculate RQs after ecotoxicity plant values were entered into the program. These were compared to the USEPA's LOCs.

Toxicity tests showed that use of ethofumesate could impact both seedling emergence and vegetative vigour of vascular terrestrial plants. Since ethofumesate was reported to be mobile, there could be potential for runoff to adversely affect off-target plants, and the potential for spray drift as well. Based on predicted EECs using maximum label application rates for sugar beets and available toxicity data, there were exceedances of the LOCs for acute terrestrial non-endangered and endangered plant species for both monocots and dicots

After characterizing the ecological risks to ethofumesate, the USEPA concluded that risks to endangered freshwater fish could be mitigated through spray drift and runoff controls or a rate reduction, while potential risks to non-target terrestrial plants could be mitigated through rate reductions.

Based on this, the USEPA required a rate reduction for aerial application to sugar beets, and spray drift and runoff precautionary statements.

The ecological risk assessment performed by the USEPA was based on a number of scenarios: Minnesota sugar beets, California sugar beets, Florida vegetable, Oregon grass seed, Pennsylvania turf, and Florida turf. The Minnesota and California sugar beet scenarios used a maximum application rate of 4.2 kg a.i./ha at 1 application/yr which encompasses the Canadian maximum seasonal application rate of ethofumesate. Based on this, the USEPA mitigation measures relating to ground application should be adapted to the Canadian situation as follows:

- To mitigate runoff, an advisory statement.
- To protect aquatic habitats, a spray drift advisory statement.
- The PMRA will require terrestrial and aquatic buffer zones for end-use products of ethofumesate used as liquids to protect aquatic organisms and terrestrial plants from spray drift. Interim buffer zones for aquatic habitats were established for ethofumesate based on data available in the USEPA RED as there were insufficient aquatic plant ecotoxicity data available.

Proposed label amendments are listed in Appendix IV. Inputs to buffer zone models are described in Appendix V.

3.2.2 Toxic Substances Management Policy Considerations

The management of toxic substances is guided by the Federal Government's *Toxic Substances Management Policy*, which puts forward a preventive and precautionary approach to deal with substances that enter the environment and which could harm the environment or human health. The policy gives decision makers direction and sets out a science-based management framework to ensure that federal programs are consistent with its objectives. One of the key management objectives is virtual elimination from the environment of toxic substances that result predominantly from human activity and that are persistent and bioaccumulative. These substances are referred to in the policy as Track 1 substances.

The Federal Toxic Substances Management Policy and the Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*, were taken into account during the re-evaluation of ethofumesate with the following conclusions:

- Ethofumesate is not bioaccumulative; the *n*-octanol–water partition coefficient (log K_{ow}) is 2.7, which is below the TSMP Track 1 cut-off criterion of ≥ 5.0. Ethofumesate does not meet all Track 1 criteria, and thus it is not a candidate for Track 1 classification.

- Based on a review of the available chemistry information (see Section 2.1), the technical product is not expected to contain impurities of toxicological concern as identified in Regulatory Directive DIR98-04 or TSMP Track 1 substances as identified in Regulatory Directive DIR99-03, Appendix II.

- Formulant issues are being addressed through PMRA formulant initiatives and Regulatory Directive DIR2006-02, *Formulants Policy and Implementation Guidance Document,* published on 31 May 2006.

4.0 Proposed Regulatory Decision

The PMRA has determined that ethofumesate is acceptable for continued registration with the implementation of the proposed risk reduction measures. These measures are required to further protect human health and the environment. Canadian end-use product labels should be amended to include label statements listed in Appendix IV. A submission to implement label revisions will be required within 90 days of finalization of the re-evaluation decision. The registrant of the technical active ingredient is required to submit data as a condition of continued registration under Section 12 of the PCPA. Appendix I lists data requirements.

5.0 Supporting Documentation

PMRA documents, such as Regulatory Directive DIR2001-03, and DACO tables can be found on our website at www.pmra-arla.gc.ca. PMRA documents are also available through the Pest Management Information Service. Phone: 1-800-267-6315 within Canada or 1-613-736-3799 outside Canada (long distance charges apply); Fax: 613-736-3798;
E-mail: pmra_infoserv@hc-sc.gc.ca.

The federal TSMP is available through Environment Canada's website at www.ec.gc.ca/toxics.

The USEPA RED document (Ethofumesate, EPA Case No. 2265) is available on the 'Office of Pesticide Programs' website at www.epa.gov/pesticides/reregistration/status.htm under Chemical Status.

List of Abbreviations

a.i.	active ingredient
ARfD	acute reference dose
CAS	Chemical Abstracts Service
aPAD	acute population adjusted dose
cPAD	chronic population adjusted dose
DEEM	Dietary Exposure Evaluation Model (a modelling program)
DWLOC	drinking water level of concern
EDWC	estimated drinking water concentration
EEC	estimated environmental concentration
EXAMS	Exposure Analysis Modeling System
FIRST	FQPA Index Reservoir Screening Tool (a modelling program)
FQPA	*Food Quality Protection Act*
g	gram
ha	hectare
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram
K_d	adsorption coefficient
K_{ow}	*n*-octanol–water partition coefficient
L	litre
LC_{50}	median lethal concentration
LOC	level of concern
LOD	limit of detection
LOAEL	lowest observed adverse effect level
mg	milligram
ml	millilitre
MOE	margin of exposure
MRL	maximum residue limit
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
PPE	personal protective equipment
PRZM	Pesticide Root Zone Model
RED	Re-registration Eligibility Decision
REI	restricted-entry interval
RQ	risk quotient
SCI-GROW	Screening Concentration In Ground Water (a modelling program)
TGAI	technical grade active ingredient
TSMP	Toxic Substance Management Policy
USEPA	United States Environmental Protection Agency
UV	ultraviolet

Appendix I Additional Data Requirements

In order for the PMRA to complete aquatic buffer zone calculations, the following data are required as a condition of continued registration under Section 12 of the *Pest Control Products Act*. The registrants are required to provide these data or an acceptable scientific rationale within the timeline specified in the decision letter that will be sent to registrants of the technical active ingredients by the PMRA:

- DACO 9.8.2: Freshwater Algae (a diatom and a blue-green algae study are required), and
- DACO 9.8.3: Marine Algae (a marine diatom species).

These studies must be conducted according to the appropriate OPPTS guidelines indicated. Should the registrant fail to submit these studies within the specified timeline, conservative buffer zones for the protection of sensitive aquatic habitats will be required on product labels.

Appendix II Registered Ethofumesate Products as of June 2007

Registration Number	Marketing Class	Registrant	Product Name	Formulation Type	Guarantee (%)
14696	Commercial	Bayer Crop Science Inc.	Nortron EC Emulsifiable Liquid Herbicide	Emulsifiable Concentrate	180 g/L
17293	Commercial	Bayer Crop Science Inc.	Nortron SC Sugar Beet Herbicide	Suspension	480 g/L
20364	Technical	Bayer Crop Science Inc.	Ethofumesate Technical Herbicide	Solid	97.7%
28117	Technical	United Phosphorous Inc.	Etho Tech Herbicide	Solid	98%
28350	Commercial	United Phosphorous Inc.	Etho SC Herbicide	Suspension	480 g/L

Appendix III Toxicological Endpoints Selected by the USEPA for Ethofumesate Health Risk

Exposure Scenario (route and period of exposure)	Dose (mg/kg bw/day)	Study	Target UF/SF or MOE or Q* [a]
Acute Dietary (females 13–49 years of age)	NOAEL = 30	Developmental toxicity study in rabbits	100
	ARfD = 0.3 mg/kg bw/day aPAD = 0.3 mg/kg bw/day		
Chronic Dietary (females 13–49 years of age)	NOAEL = 30	Developmental toxicity study in rabbits	100
	cRfD = 0.3 mg/kg bw/day cPAD = 0.3 mg/kg bw/day		
Chronic Dietary (general population including infants and children)	NOAEL = 127	Chronic oral toxicity/carcinogenicity study in rat	100
	cRfD = 1.3 mg/kg bw/day cPAD = 1.3 mg/kg bw/day		
Dermal (all durations) - (female 13–49 years of age)	NOAEL = 30	Developmental toxicity study in rabbits	100
Dermal - Short- and Intermediate term (general population including infants and children)	NOAEL = 190	90-day oral toxicity study in rat	100
Dermal - Long-term	NOAEL = 127	Chronic oral toxicity/carcinogenicity study in rat	100
Inhalation (All durations) - (female 13–49 years old)	NOAEL = 30	Developmental toxicity study in rabbits	100
Inhalation - Short- and Intermediate term (general population including infants and children)	NOAEL = 190	90-day oral toxicity study in rat	100
Inhalation - Long-term - (general population including infants and children)	NOAEL = 127	Chronic oral toxicity/carcinogenicity study in rat	100
Cancer (oral, dermal, inhalation)	Classification: "Not likely to be carcinogenic to humans."		

[a] UF/SF refers to total of uncertainty and/or safety factors for dietary assessments, MOE refers to desired margin of exposure for occupational or residential assessments; Q* refers to cancer potency factor

Appendix IV Label Amendments for Products Containing Ethofumesate

Canadian end-use product labels should be amended to include the following statements to further protect workers and the environment.

I) The following statements should be included in a section entitled "PRECAUTIONS":

- "Wear a long-sleeve shirt, long pants, shoes plus socks during mixing, loading, application, clean-up and repair activities. In addition wear chemical-resistant gloves during mixing, loading, clean-up and repair activities."

- "Do not enter or allow worker entry intro treated areas during the restricted-entry interval (REI) of 12 hours."

II) The following statements should be included in the section entitled "DIRECTIONS FOR USE":

- "DO NOT apply this product directly to freshwater habitats (such as lakes, rivers, sloughs, ponds, prairie potholes, creeks, marshes, streams, reservoirs, ditches and wetlands), estuaries or marine habitats. DO NOT contaminate irrigation or drinking water supplies or aquatic habitats by cleaning of equipment or disposal of wastes."

  "Field sprayer application: **DO NOT** apply during periods of dead calm. Avoid application of this product when winds are gusty. **DO NOT** apply with spray droplets smaller than the American Society of Agricultural Engineers (ASAE) medium classification."

  "Buffer zones:

  The buffer zones specified in the table below are required between the point of direct application and the closest downwind edge of sensitive terrestrial habitats (such as grasslands, forested areas, shelter belts, woodlots, hedgerows, rangelands, riparian areas and shrublands) and sensitive freshwater habitats (such as lakes, rivers, sloughs, ponds, prairie potholes, creeks, marshes, streams, reservoirs, ditches and wetlands).

Method of application	Buffer Zones (metres) Required for the Protection of:			
	Freshwater Habitat of Depths:			Terrestrial habitat
	Less than 1 m	1 to 3 m	Greater than 3 m	
Field sprayer	1	0	0	2

When a tank mixture is used, consult the labels of the tank-mix partners and observe the largest (most restrictive) buffer zone of the products involved in the tank mixture."

III) The following statements should be included in a section entitled "ENVIRONMENTAL HAZARDS"

- "To reduce runoff from treated areas into aquatic habitats, consider the characteristics and conditions of the site before treatment. Site characteristics and conditions that may lead to runoff include, but are not limited to: heavy rainfall, moderate to steep slope, bare soil, poorly draining soil (e.g. soils that are compacted, fine textured, or low in organic matter such as clay)."
- "Avoid application of this product when heavy rain is forecast."
- "TOXIC to aquatic organisms and terrestrial plants. Observe buffer zones specified under DIRECTIONS FOR USE."

The label amendments presented above do not include all label requirements for individual end-use products, such as first aid statements, disposal statements, precautionary statements, and supplementary protective equipment. Additional information on labels of currently registered products should not be removed unless it contradicts the above label statements.

A submission to request label revisions will be required within 90 days of finalization of the re-evaluation decision.

Appendix V Inputs to Buffer Zone Models

Ground Use Data (from Canadian labels)				
Crop	**Formulation Type**	**Method of Application**	**Number of Application**	**Maximum Application Rate (g a.i./ha)**
Sugar beets	Emulsifiable concentrate	Field sprayer (medium)	1	3960
Sugar beets	Suspension	Field sprayer (medium)	1	3960

Model Input Data for Aquatic Buffer Zones (from 2005 RED)		
Half life for aquatic buffer zones	water and sediment	*156 days*
Most sensitive freshwater species	Rainbow trout	1/10 LC_{50} = 0.075 mg a.i./L
Most sensitive estuarine/marine species	Eastern oyster	NOAEC = 0.8 mg a.i./L

Model Input Data for Terrestrial Buffer Zones (from 2005 RED)		
Half life for terrestrial buffer zones	Soil degradation half-life	253 days
Most sensitive terrestrial plant species EC_{25} for vegetative vigour	Soybean – Vegetative vigour	100 g a.i./ha